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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,402	08/03/2001	Peter Hofert	SCH 1808	9208

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,402	HOFERT ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2004 and 04 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5,7,8,10-16 and 18-23* is/are pending in the application.

4a) Of the above claim(s) *8,12 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,7,10,11,13-16,18-20,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 29, 2004 has been entered.

Status of the Claims

Claims 1 and 17 have been canceled. Claims 1-5, 7, and 10, 14-16, 19, 20, and 22 have been amended. Claim 23 has been added. Claims 2-5, 7, 8, 10-16, and 18-23 are pending. Claims 8 and 12 were previously withdrawn pursuant to a restriction requirement. Claim 21 depends from claim 12 and is likewise withdrawn. Any rejection or objection or rejection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 5 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites ratios of the gestagen and CD. However, the claim does not state if the ratios are weight or molar, rendering the claim vague and indefinite.

Claim 15 depends from canceled claim 1. Further regarding this claim, the claim recites, "precipitating a β–cyclodextrin or a γ–cyclodextrin into a gestagen . . ." It is not clear what Applicant contemplates in "precipitating a cyclodextrin into a gestagen." For these reasons, the claim is rendered vague and indefinite.

Claim Rejections - 35 USC § 103

Claims 2-5, 7, 10, 11, 13-16, 18-20, 22, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over SCHOLLKOPF et al (WO 96/20209) and BACKENSFELD et al (US 5,798,338) in view of HEDGES (Chem. Rev., 1998).

The invention is drawn to a combination, including a pharmaceutical composition, comprising a gestagen of Formula I with a cyclodextrin. Dependent recite species of gestagens and CDs and ratios of the components and methods of preparing the combination.

Applicant's arguments filed September 29, 2004 have been fully considered but they are not persuasive. The declaration under 37 CFR 1.132 filed November 4, 2004 is insufficient to overcome this rejection. The contents of the declaration are discussed below.

Schollkopf teaches the gestagens of Formula I. See col 1-4. The species recited in claims 3 and 20 is disclosed at col 4, lines 9-10. The reference further teaches that the disclosed compounds have high activity and can be used in low dosages, alone or in combination with estrogens to prepare compositions having utility as oral contraceptives. See col 4, beginning line 8, and continuing through col 5, line 18. See also, reference claims 12-14. The reference also

suggests the addition of solubilizers to enhance solubility of the compounds. See col 6, lines 19-21.

The reference does not teach the combination of gestagens with CDs or methods of preparing such a combination.

Backensfeld teaches the preparation of solid dosages of sex hormones but notes drawbacks in such preparations, such as the reduction of the active ingredient due to oxidative degradation. See col 1, lines 1-27. The disadvantages of such dosage forms apply to sex hormones in general, including estrogens and gestagens. See col 1, lines 34-49. The reference teaches that such drawbacks can be reduced or avoided by preparing CD clathrates of the active ingredient hormone(s)--that is, the active ingredients would be stabilized with respect to oxidative degradation. See col 1, lines 28-33. The reference further suggests CD species, ratios of the components, and methods or preparing compositions. See col 2, lines 8-62. The reference does not describe a process as "trituration," but the described process of kneading the components would be essentially the same as trituration. The examples exemplify adding an ethanolic solution of the steroidal hormone to an aqueous solution of CD to form a complex (co-crystallization) and pressing said complex into tablets. See examples 1-4.

Methods for preparing CD complexes with small molecules are well known in the art. Hedges teaches several methods. See Section I, pp 2025-6. Hedges also notes that CDs are well known for solubilizing and stabilizing pharmaceutical products. See Table 1 and page 2038, 1st full paragraph.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare CD complexes of the gestagens of Formula I in the form of oral

dosages for their art-disclosed utility. The artisan would be motivated to prepare such a complex in order to reduce oxidative degradation that is known to occur in steroidal sex hormones and to increase solubility of the steroidal agents. The artisan would be particularly motivated to select any specific embodiment disclosed by Schollkopf. It would be within the scope of the artisan to select any appropriate CD and ratio of components through routine experimentation. It would be further obvious to use such a product as an oral contraceptive because Schollkopf had taught this utility.

Hedges has established that preparation of such complexes by a number of methods is routine, so in the absence of unexpected results, it would be within the scope of the artisan to select any known method of preparation and further to pelletize the prepared complexes into tablets.

Applicant has submitted a declaration with data that purport to demonstrate unexpected results. Declarant states that the compounds complexed with a CD are significantly more stable than those not complexed. As discussed above, Backensfeld had taught the CDs have the capacity to stabilize gestagens. Therefore, the finding is not unexpected. The art does not teach the prevention of an acyloin rearrangement, but it appears that Declarant has recognized another advantage that would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

As noted, the art does not teach prevention of an acyloin rearrangement, but from the results presented, the rate of degradation due to oxidation vs. rearrrangement cannot be determined. The rearrangement may be much faster or trivial compared to competing oxidation. Therefore, if it were determined that a compound of Formula I achieved relatively greater

stabilization vs. an equivalent compound without a hydroxy at position 21, this would be considered unexpected result. An appropriate comparison, for example, would be ZK 187226 vs. a structurally analogous compound wherein $R^{21'}$ is H or lower alkyl (such as in the original claims).

As an aside, for the purposes of calculating amounts of degradation, the examiner would not consider rearrangement of '226 to '225 to be degradation. Because there is no defined stereochemistry at position 21, '225 and '226 would be the same compound under Formula I.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Wednesday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier

Leigh C. Maier
Patent Examiner
December 3, 2004